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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,757	02/11/2005	Hiroyuki Yano	265980US0PCT	6892
22850	7590	01/02/2008		
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER VENC, DAVID J	
			ART UNIT	PAPER NUMBER
			1641	
			NOTIFICATION DATE	DELIVERY MODE
			01/02/2008	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com  
oblonpat@oblon.com  
jgardner@oblon.com

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/524,757	YANO ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on October 10, 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 5-9 and 14-17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4, 10-13 and 18 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-18 are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on October 10, 2007 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>10/10/07</u> . | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Election/Restrictions*

Amended claims 5-9 and 14-17 are directed to an invention that is not linked to form a single general inventive concept under PCT Rule 13.1. Restriction is required under 35 U.S.C. 121 and 372.

- I. Claims 1-4 and 13, drawn to a special technical detection method.
- II. Claims 5-9 and 14-17, drawn to a special technical screening method.
- III. Claims 10-12 and 18, drawn to special technical kits.

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. Here, the kits of Invention III are used in the methods of Inventions (I or II). However, the technical feature linking the inventions does not constitute a special technical feature as defined by PCT Rule 13.2 because the technical feature does not define a contribution over the prior art. Specifically, Kosower & Kosower, 251 METHODS ENZYMOL. 133 (1995), teach all the kit components of Invention III, including an SH group-protecting agent (see p. 142, Section [C], "reactive thiols are first blocked") and an SH group-detecting substance (see p. 142, Section [C], "followed by mBBR").

Therefore, unity of invention is lacking because the technical feature linking the inventions does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

Since Applicants have received an action on the merits for the originally presented invention corresponding to Inventions I and III, these inventions are constructively elected by original presentation

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for prosecution on the merits. Accordingly, claims 5-9 and 14-17 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Currently, claims 1-4, 10-13 and 18 are under examination.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Kosower & Kosower, 251 METHODS ENZYMOL. 133 (1995).

Kosower & Kosower describe a method for detecting disulfide ( $\text{—S—S—}$ ) bonds in a protein sample comprising both  $\text{—S—S—}$  bonds and sulfhydryl ( $\text{—SH}$ ) groups, the method comprising:

1. adding a  $\text{—SH}$  group protecting agent to the protein sample (see p. 142, Section [C], "reactive thiols are first blocked");
2. adding a reducing agent to the proteins, thereby reducing the  $\text{—S—S—}$  bonds and creating a new set of  $\text{—SH}$  groups on the proteins (see p. 142, Section [C], "Samples are then treated with DTT to reduce the disulfides");
3. detecting the new set of  $\text{—SH}$  groups on the proteins, thereby detecting  $\text{—S—S—}$  bonds in the protein sample (see p. 142, Section [C], "followed by mBBR"; see *also*, p. 145, second full paragraph, "fluorescent and stained protein bands").

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kosower & Kosower, 251 METHODS ENZYMOL. 133 (1995), in view of O'Farrell, 250 J. BIOL. CHEM. 4007 (1975).

Kosower & Kosower describe a method for detecting disulfide bonds as substantially described *supra*.

Kosower & Kosower do not describe a method incorporating "two-dimensional" electrophoresis.

However, O'Farrell describes two-dimensional electrophoresis for separating and analyzing proteins in complex mixtures (see Summary).

It would have been obvious for persons of ordinary skill to use two-dimensional electrophoresis with the Kosowers' method because O'Farrell says two-dimensional electrophoresis improves upon the resolving ability of one-dimensional electrophoresis by providing the ability to resolve proteins differing in both isoelectric point and molecular weight (see Summary and Introductory paragraphs), which Examiner posits, will help the Kosowers resolve their native protein from the various alkylated, reduced, mBBBr-labeled and/or thiolated derivatives their method produces.

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Claims 4, 11 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kosower & Kosower, 251 METHODS ENZYMOL. 133 (1995), in view of Görg *et al.*, 8 ELECTROPHORESIS 122 (1987).

Kosower & Kosower describe a method for detecting disulfide bonds as substantially described *supra*.

Kosower & Kosower do not describe a method incorporating "iodoacetamide".

However, Görg *et al.* used "iodoacetamide" to help visualize proteins in silver-stained polyacrylamide gels (see Fig. 2C)

It would have been obvious for persons of ordinary skill to use "iodoacetamide" with the Kosowers' method because Görg *et al.* say DTT contributes to streaking in silver-stained polyacrylamide gels (see Fig. 1) and discovered that iodoacetamide works best for eliminating these streaks, probably by reacting with excess DTT (see p. 123, left column, first full paragraph), which Examiner posits, will help the Kosowers resolve their native protein from the various alkylated, reduced, mBBR-labeled and/or thiolated derivatives in the presence of DTT.

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Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kosower & Kosower, 251 METHODS ENZYMOL. 133 (1995), and O'Farrell, 250 J. BIOL. CHEM. 4007 (1975), as applied to claim 3, and further in view of Gorg *et al.*, 8 ELECTROPHORESIS 122 (1987).

Kosower & Kosower and O'Farrell describe a method for detecting disulfide bonds as substantially described *supra*. These people do not describe a method incorporating "iodoacetamide".

However, Görg *et al.* used "iodoacetamide" to help visualize proteins in silver-stained polyacrylamide gels (see Fig. 2C)

It would have been obvious for persons of ordinary skill to use "iodoacetamide" with the Kosowers' method because Görg *et al.* say DTT contributes to streaking in silver-stained polyacrylamide gels (see Fig. 1) and discovered that iodoacetamide works best for eliminating these streaks, probably by reacting with excess DTT (see p. 123, left column, first full paragraph), which Examiner posits, will help the Kosowers resolve their native protein from the various alkylated, reduced, mBBR-labeled and/or thiolated derivatives in the presence of DTT.



***Response to Arguments***

***Claim Rejections - 35 USC § 112***

In prior Office Action, claims 1 and 5 were rejected under 35 U.S.C. 112, second paragraph, for appearing incomplete or omitting essential steps, such omission amounting to a gap between the steps. Specifically, the sequential steps of "modifying" immediately followed by "cleaving" was considered indefinite because the purpose of "modifying" was not clear (*i.e.*, one or more steps pertaining to doing something with the modified protein after performing the step of "modifying" appeared omitted from the claim).

In response, Applicants amend claim 1 to add a new set of —SH groups on the proteins, wherein Applicants intend "to prevent from detection" this new set of —SH groups. Applicants' amendment is sufficient to overcome this rejection. Accordingly, this rejection is withdrawn.

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In prior Office Action, claims 9, 14, 16 and 17 were rejected under 35 U.S.C. 112, second paragraph, because the phrase "house dust" is indefinite (*i.e.*, the composition of "house dust" is not clear). Herein, claims 5-9 and 14-17 are withdrawn from consideration as being directed to a non-elected invention. Applicants' argumentation on this issue will be considered upon rejoinder of withdrawn claims 5-9 and 14-17.

***Claim Rejections - 35 USC § 102***

In prior Office Action, claims 1-8, 10-13, 15 and 18 were rejected under 35 U.S.C. 102(b) as being anticipated by Wiktorowicz & Raysberg (US 6,214,191). And, claims 1, 2, 4-6, 8-18 were rejected under 35 U.S.C. 102(b) as being anticipated by Buchanan *et al.* (US 5,952,034).

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In response, Applicants amend claim 1 to add a new set of —SH groups on the proteins, wherein Applicants intend "to prevent from detection" this new set of —SH groups. Applicants' amendment is sufficient to overcome this rejection. Accordingly, this rejection is withdrawn.

**Conclusion**

No claims are allowable at this time.


The prior art made of record, but not relied upon, is considered pertinent to applicant's disclosure.

Hashimoto *et al.*, 129 ANAL. BIOCHEM. 192 (1983), are cited for their discovery that iodoacetamide improves silver-stained one-dimensional polyacrylamide gels, relevant to claims 4, 11 and 13.

Smith *et al.*, 14 BIOCHEMISTRY 766 (1975), are cited for their teaching of the "temporary" nature of —SH group protecting agents, relevant to claims 1-4, 10-13 and 18.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

  
LONG V. LE 02/21/07

**SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600**

David J Venci  
Assistant Examiner  
Art Unit 1641

djv